Global identification of transcriptional regulators of pluripotency and differentiation in embryonic stem cells.

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Public Summary:
The embryonic stem cells have the capability to undergo unlimited self-renewal and differentiate into all cell types in the body. The study presented here identify the transcriptional network required to maintain the pluripotency of human ES cells.

Scientific Abstract:
Human embryonic stem cells (hESCs) hold great promise for regenerative medicine because they can undergo unlimited self-renewal and retain the capability to differentiate into all cell types in the body. Although numerous genes/proteins such as Oct4 and Gata6 have been identified to play critical regulatory roles in self-renewal and differentiation of hESC, the majority of the regulators in these cellular processes and more importantly how these regulators co-operate with each other and/or with epigenetic modifications are still largely unknown. We propose here a systematic approach to integrate genomic and epigenomic data for identification of direct regulatory interactions. This approach allows reconstruction of cell-type-specific transcription networks in embryonic stem cells (ESCs) and fibroblasts at an unprecedented scale. Many links in the reconstructed networks coincide with known regulatory interactions or literature evidence. Systems-level analyses of these networks not only uncover novel regulators for pluripotency and differentiation, but also reveal extensive interplays between transcription factor binding and epigenetic modifications. Especially, we observed poised enhancers characterized by both active (H3K4me1) and repressive (H3K27me3) histone marks that contain enriched Oct4- and Suz12-binding sites. The success of such a systems biology approach is further supported by experimental validation of the predicted interactions.